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Enablers and barriers to newborn screening for sickle cell disease in Africa: results from a qualitative study involving programs in six countries

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Title: Enablers and barriers to newborn screening for sickle cell disease in Africa: results from a qualitative study involving programs in six countries

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Abstract

Objectives: Given the fundamental role of newborn screening (NBS) to enable prompt diagnosis and optimal clinical management of individuals with sickle cell disease (SCD), we sought to systematically assess enablers and barriers to implementation of NBS programs for SCD in Africa using established qualitative research methods.

Setting: Childbirth centers and newborn screening laboratories in East, West, and Southern Africa.

Participants: Program leaders involved with establishing and operating NBS programs for SCD in Angola, Democratic Republic of Congo, Ghana, Liberia, Nigeria, and Tanzania.

Primary and Secondary Outcome Measures: Data obtained through a structured, phased interview approach were analyzed using a combination of inductive and deductive codes and used to determine primary themes related to the implementation and sustainability of SCD NBS programs.

Results: Four primary themes emerged from the analysis relating to governance (e.g., pragmatic considerations when deploying overcommitted clinical staff to perform NBS), technical (e.g., design and execution of operational processes), cultural (e.g., variability of knowledge and perceptions of community-based staff), and financial (e.g., issues that can arise when external funding may effectively preclude government inputs) aspects. Key learnings included perceived factors that contribute to long-term NBS program sustainability.

Conclusions: The establishment of enduring NBS programs is a proven approach to improving the health of populations with SCD. Organizing such programs in Africa is feasible but initial implementation does not assure sustainability. Our analysis suggests that future programs should prioritize government partner participation and funding from the earliest stages of program development.

Summary Box

What is already known?

- Newborn screening combined with comprehensive clinical care services prevents early sickle cell disease-associated deaths
- There are no national-level newborn screening programs in Africa despite the initiation of pilot programs in multiple countries
- Enablers and barriers to successful implementation and sustainability have not previously been systematically characterized

What are the new findings?

- Newborn screening programs for sickle cell disease are technically feasible to implement in Africa
- Program design should be informed by a comprehensive understanding of local staffing and workflow factors in order to achieve practical and sustainable implementation
- Government involvement, including funding, is an integral element of success

What do the new findings imply?

- Early introduction of sickle cell disease newborn screening programs in Africa does not assure sustainability, in particular if funded by external sources.
- Future sickle cell disease newborn screening programs should prioritize government partner participation and funding from the earliest stages of program development

Article Summary

Strengths and limitations of this study

Strengths

- This is one of the largest studies of enablers and barriers to successful implementation and sustainability of sickle cell disease newborn screening programs in Africa, where no national-level programs currently exist.
- Applying established qualitative research methods, this study investigated the firsthand experiences of clinical and coordinating leaders involved in establishing and operating programs in six African countries: Angola, Democratic Republic of Congo, Ghana, Liberia, Nigeria, and Tanzania.

Limitations

- Six programs were included in the analysis, which is a sample of the total number of newborn screening programs for sickle cell disease that have been implemented in Africa
- By design, a single or small number of participants were surveyed from each program
- The lessons learned from one country may not always be immediately transferable to other countries due to various local factors.

Introduction

Sickle cell disease (SCD) is one of the world's commonest hemoglobinopathies, estimated to affect in excess of 400,000 newborns annually with 80% of patients born into populations living in low and middle-income countries.[1,2] The disease is caused by a single point mutation in the beta-globin gene that results in the formation of sickle hemoglobin (hemoglobin S, or HbS).[3] Under certain conditions including hypoxia, HbS polymerizes and creates distorted (i.e., "sickle"-shaped), adherent, and less deformable red blood cells (RBCs).[4] The result is easily-hemolyzed RBCs with a shortened lifespan, endothelial damage, vessel obstruction, and other pathophysiological effects that collectively contribute to the development of a vast constellation of acute and chronic clinical manifestations and, often, premature mortality.

Fetal hemoglobin (HbF), the predominant hemoglobin during gestation and in neonates, is the most potent known inhibitor of HbS polymerization. As such, infants with SCD are asymptomatic until HbF levels decline to low levels, typically within the first 6-24 months of life. Early diagnosis prior to the predominance of HbS is critical to allow for provision of early lifesaving interventions. Since SCD cannot be diagnosed by clinical signs at birth, newborn screening (NBS) materialized decades ago to be a standard approach in many high-resource countries for identifying babies with SCD before complications develop.[5,6] Early detection enables the prompt initiation of parental education and evidence-based preventative care practices that include penicillin prophylaxis and pneumococcal vaccination.[7,8]

In the 1980s, a randomized, placebo-controlled trial in the United States confirmed the efficacy of penicillin prophylaxis in significantly reducing incidence of and mortality due to *Streptococcus pneumoniae*, the leading cause of death in young children with SCD.[5] Evidence from that study provided the impetus for the U.S. National Institutes of Health Consensus Development Conference on Newborn Screening for SCD and Other Hemoglobinopathies to recommend that all babies born in the United States be screened for SCD.[9] In the United States, where universal newborn screening for SCD (i.e., testing newborn babies within the first few weeks after birth) has existed in all 50 states since 2006, NBS is largely acknowledged to be among the most important factors leading to high rates (well over 90%) of survival into adulthood.[5,10] Universal screening for SCD now constitutes national policy in the United States, Brazil, United Kingdom, Germany, Spain, Netherlands, and Malta;[11–14] longstanding NBS programs have also been in place in other parts of Europe, Jamaica, Ghana and Canada.[12,15,16] Targeted screening of newborns (e.g., according to ancestry), is implemented in some regions but has been shown to be less effective compared with universal screening at identifying infants with disease and preventing deaths.[17]

The vast majority of people with SCD globally are born in Africa where up to 2% or more of births are reported to be affected in some regions, contributing silently but significantly (8-16%) to under 5 mortality in high burden countries.[18–20] While no country in Africa has yet implemented policies for universal screening, various national NBS programs for SCD have been organized, and with heightened awareness about the impact of the disease there is optimism for increased progress in the future.[18,19,21–25] In this context we sought to characterize the enablers and challenges to conducting NBS for SCD based on the experiences of previous and ongoing programs. Specifically, we assessed programs in Angola, Democratic Republic of Congo (DRC), Ghana, Liberia, Nigeria, and Tanzania.[18,19,22–24,26] Using established qualitative research methods,[27–29] we conducted semi-structured interviews with clinical and coordinating leaders involved in each program and extracted key messages to codify main lessons learned. This analysis is envisioned to be a resource for patients, clinicians, policymakers, and other stakeholders seeking to improve health systems relating to newborn screening for SCD in Africa and other limited resource settings globally where SCD occurs in high prevalence.

Methods

Study design

We conducted semi-structured interviews with individuals who were responsible for, or significantly involved in, the design and implementation of NBS programs for SCD in an African country (hereafter referred to as "participants"). The purpose of the interviews was to describe the process for designing and implementing the programs, identify enablers and challenges, and elicit lessons learned in order to facilitate a concise summary of learnings that could be used to inform future SCD NBS programs. Additionally, participants provided background information about their program by email in advance of their interview. If a participant did not provide the information prior to their interview, then these questions were asked at the start of the interview. See Supplemental Materials for the background questions and interview guide.

Interviews were conducted in two phases. The first phase included four participants (representing programs in Ghana, Angola, DRC, and Liberia), who answered a comprehensive set of questions about their programs. Interviews were transcribed, coded and analyzed after the first phase of data collection. From this analysis, the study team identified aspects of SCD NBS program that warranted deeper exploration either because they emerged as critical to the success of the program or because they were characterized by variability that prompted deeper investigation across programs. The latter included aspects of the program that were subjective (e.g., cultural attitudes towards SCD) as opposed to mechanistic (e.g., the type of test used to screen for SCD). The second phase included 2 participants (representing programs in Nigeria and Tanzania) who answered questions on the topics determined in phase 1 that required further discussion. By limiting the number of questions asked in the second phase, the study team was able to conduct deeper exploration of each of the topics. The findings from phase two supplemented the results from the corresponding topics in phase 1. The results from the two phases were analyzed together to identify key learnings for the establishment and maintenance of SCD NBS programs in Africa.

Patient and Public Involvement

Patients were not involved in this study. Participants were identified by study members as program leaders after reviewing publications related to SCD NBS in African countries. Participants were recruited by email. During the recruitment, all participants , program leaders that were interviewed, and reported various levels of public engagement in their respective countries. They were invited to review the results and to contribute to identifying key messages and implications of the results, clarify or correct any information from their interviews, and co-author the resulting manuscript (i.e., in alignment with a form of "member checking" described in the literature).[30]

Interview guide

We designed the interview guide to gain insight into how participants developed, implemented and, when applicable, sustained their program. The guide was created with input from study team members with general expertise on SCD, SCD NBS programs in Africa, and a qualitative researcher (NH). Collectively, the study team identified the key steps of establishing and implementing a screening program as well as other factors that were likely to impact the success of the program. These high-level topics included: program partners, planning the program, launching the program, logistics of day-to-day operations, establishing and running the laboratory, patient notification and follow-up, funding and costs, program disposition, and perceptions of the program by families of newborns. The interview guide was piloted with a member of the study team (KOF) for clarity, flow, and duration. Minor revisions to the interview guide were made based on his feedback and his responses were included in the dataset.

Data collection and analysis

Participants were interviewed one time for approximately 1 hour. Phase one interviews took place between October and December 2017. Phase two interviews took place between July and September 2019. All interviews were conducted by phone, audio recorded, and transcribed.

We performed a thematic analysis of the interviews using a coding scheme developed with a combination of inductive and deductive codes. In phase one, coding was performed in NVivo (QSR) and the content from each code was summarized in a table, including key quotes and identification of key findings. Key findings were used to identify areas that required more in-depth exploration during the second phase of data collection. Phase two interviews were analyzed by directly adding key findings into the summary tables from Phase one. Results were shared with the participants for feedback and, if needed, corrections, clarifications, and the addition of missing information.

Ethics

The Institutional Review Board of Boston Children's Hospital reviewed the study and determined that this project meets the criteria for exemption. We obtained active consent before the start of every interview.

Results

Study sample

The study involved data collection relating to NBS programs in six countries in Africa (Figure 1) with representation from West (Ghana, Liberia, Nigeria), Central (Angola, Democratic Republic of Congo), and East Africa (Tanzania). Participants were based at academic institutions and professional societies; many had worked in conjunction with government agencies and external collaborators. The planning period before the initiation of screening ranged from approximately 9 months to 4 years, and the duration of screening ranged from 21 months to 25 years. The number of birth centers involved in the NBS programs ranged from one to approximately 250. Most programs are ongoing in some capacity, albeit several with reported periods of inactivity due to various operational challenges as described below.

Qualitative findings

Four primary themes emerged in the analysis relating to (a) structural and governance aspects; (b) technical aspects; (c) cultural aspects; and (d) financial aspects. Within these four main themes we identified 12 sub-themes that are summarized in Table 1 and described below. A summary of major lessons learned/recommendations is provided in Table 2.

Primary theme I: Structural and governance aspects

The role of national health authorities was universally felt to be a critical determinant of success. Government entities, including Ministries of Health and/or other national health service delivery units, were involved in each of the programs with a level of engagement that ranged along a continuum from passive (e.g., conceptual "support" of the program and allowance to proceed without allocating new resources) to active (e.g., recognizing the NBS program as a core part of the health system and providing clinical staff and other resources to maintain its continuity). While in several countries the government was involved from the early stages of NBS program design, in no country was the government the initial actor involved in establishing the NBS program. Programs that continued beyond a "pilot" phase ascribed government involvement as a key enabler; likewise, programs that met with challenges in achieving long-term sustainability point to lack of government ownership as a main reason.

All participants reported the topic of program structure and governance to be an essential consideration. Programs were each championed by clinician-led teams with specialized expertise in caring for patients with SCD. All programs focused mainly on births taking place in public health (i.e., government-operated) facilities; private sector birth centers were less commonly included. Clinical and ancillary staff (e.g., midwives and nurses) that worked at birth centers and were responsible for the hands-on aspects of screening (i.e., conducting heelsticks, communicating with families, etc.) were generally government-employed workers who had been on staff prior to the initiation of the NBS program. In most cases, therefore, the work associated with NBS constituted a new task they were asked to perform in addition to other duties. Across the programs, coordinating staff played a fundamental role in organizing and overseeing a vast array of logistics and managing the relationships with multiple stakeholders that variably included families, birth center staff, SCD clinical experts, government representatives, and external collaborators including clinician colleagues and funding partners.

An important sub-theme relating to staffing concerned the availability of specialized clinical "Centers of Excellence" that would be capable of providing holistic preventative and treatment services for individuals that were diagnosed with SCD through the NBS programs. Participants recognized that the existence of such centers, and their accessibility to patients, was a pre-requisite to the initiation of NBS programs such that families could be immediately offered a clinical service for follow-up upon notification of positive test results.

Primary theme II: Technical aspects

While the general workflows involved in NBS programs are conceptually straightforward (e.g., sample acquisition, laboratory testing, and notification of results), the design and execution of consistent operational processes was reported by several programs to be an intensive and challenging exercise in practice. This was felt in part to be due to the very high level of coordination that was required between practitioners at birthing sites (who were responsible for collecting specimens, organizing specimen transport to the laboratory, receiving laboratory results, and notifying families), technicians in laboratories (who were responsible for receiving and testing specimens, and reporting laboratory results), and coordinators that oversaw NBS programs (responsible for ensuring adequate training of staff, reliable availability of equipment and supplies, reporting to national authorities, and other activities). In one program the laboratory was located in a different city from the birth centers, requiring the specimens to be transported by an approximately 7-hour car ride from the birthing sites to the laboratory. Another program shipped specimens in a sealed container at 4^{o}C by plane to the NBS program laboratory in another country. The ambition of most programs was to fully integrate the NBS workflows into routine health system processes; ultimately, this was achieved to a variable degree by different programs. All programs had a common aim to keep the cycle duration (i.e., from the time of specimen acquisition to the time when families were notified of results) as short as possible. One commonly cited reason for delays in the NBS workflow was in tracking down families to share laboratory results—some families were not reachable by phone, which necessitated in-person visits that were time consuming for NBS staff and not always successful.

Robust data collection and management systems were important to support workflows (i.e., registering babies that underwent testing, storing laboratory results, and keeping record of when families were notified of results), facilitate quality improvement of NBS programs (i.e., as a means to identify when the workflows were operating sub-optimally), and generate evidence that could be used for advocacy, research, or to inform health policy (e.g., incidence data, cost-effectiveness, or impact on health outcomes). Most programs utilized a hybrid model that involved some paper-based record keeping and some digital components. One of the programs (Ghana)

converted entirely to a digital “app”-based system beginning in 2018 accessible on the phones of birth attendants, laboratory technicians, and program coordinators.

All programs, except Nigeria (where high-performance liquid chromatography (HPLC was used)), used isoelectric focusing (IEF) as the primary technique for screening or diagnosis, and some programs HPLC or capillary electrophoresis for confirmatory testing after screening. While none of the programs surveyed reported that NBS laboratory equipment was a main barrier, virtually all of the programs reported challenges with maintaining regular maintenance of equipment or reliable access to reagents. In some cases, periodic unavailability of reagents led to delays in testing.

Primary theme III: Cultural aspects

Some NBS programs reported quick adoption of new technical practices by staff (e.g., conducting heelsticks and managing blood spot specimens) whereas other programs met with some challenges in fully integrating this practice due to the perception of increased workload. Some programs described clinical staff “champions” who became highly dedicated to the program (in the same way that many of the participants were), helped to advocate for the program, and trained other staff members. Ultimately, most programs reported achieving a state of cultural adaptation resulting in a sense of pride amongst the program staff for being involved in a novel program with profound implications for the health of individuals with SCD.

Community engagement was highlighted by several programs as an important determinant of success. It was reported that knowledge about SCD amongst community members varied widely and was occasionally confounded by false perceptions about the disease or stigmatization. In some cases, the cultural aspects of community engagement were noted be a determinant in the ability of NBS program staff to follow-up with families to provide notification of test results (i.e., if families were fearful of receiving results). Participants noted that families could also be dubious of positive results in the face of a baby who is healthy appearing (since babies with SCD are universally asymptomatic in early infancy).

Primary theme IV: Financial aspects

In all programs NBS services were provided free of charge to families. Participants reported an idealized scenario where NBS programs were entirely funded by local or national governments such that programs were fully integrated as part of routine public health services.

Several program leaders raised the idea of cost-sharing between NBS programs as a potential approach for reducing the costs borne by each individual program. One example that was implemented was the shipping of laboratory specimens from one country to another for testing. Another example that was raised as a concept but not yet implemented was purchasing materials such as reagents for laboratory equipment in bulk.

All programs received some form of external funding, defined as funding from out-of-country entities. Sources of external funding included foundations, non-governmental organizations, private sector companies, and governments of other countries. Many participants reported external funding to have been an important enabler in helping to establish and/or maintain operations, and in some cases the cessation of external funding resulted in the need to scale down or halt the program. External funding was therefore generally perceived to be a “double-edge sword” whereby it had been necessary for some programs to manifest but at the same time it complicated the attainment of long-term sustainability since permanent funding from outside sources was not feasible.

Discussion

Newborn screening programs constitute a standard approach for diagnosing SCD in several countries and are urgently needed in Africa to assure that affected individuals promptly receive essential counseling and preventative and therapeutic care.[2,31] The reality, however, is that the establishment and sustained operation of NBS programs in Africa is complex due to many factors. In an effort to better understand experience-based and pragmatic determinants of success, this study sought to harness lessons learned from participants involved in establishing and operating NBS programs that took place across West, Central, and East Africa. While there are numerous published reports of progress achieved with sub-national NBS programs for SCD in individual countries,[18,19,22–24] we had identified only a single previous report that analyzed cross-country experiences; that study described pilot programs in DRC and Burkina Faso and presented an excellent review of the rationale for SCD NBS programs along with high-level guidance for selected aspects of their implementation.[32] Thus, to our knowledge, the current study involving programs in six countries constitutes the first attempt to integrate learnings from a "critical mass" of NBS programs for SCD in Africa. Through standard qualitative methods, four main themes encompassing twelve sub-themes emerged that highlight enablers and barriers to implementation.

A main and crucial finding of this study was confirmation that NBS programs for SCD are feasible to successfully implement in Africa, as evidenced by the large numbers of babies screened (e.g., tens of thousands) and the long duration of screening (e.g., more than 25 years) that was demonstrated in some programs. Nevertheless, a consistent narrative emerged that feasibility did not ensure sustainability. Many of the programs reported periodic setbacks in their capabilities to maintain their planned level of operations or to expand, and some programs were forced to cease operations. In no case were technical or workflow issues the primary challenge; rather, there was general consensus that the greatest barrier to the long-term success of NBS programs resulted from their incomplete adoption into routine health systems. This was attributed mostly to inter-related aspects of governance (in particular, government involvement) and funding.

Government commitment was recognized by all interviewees as an essential element of success, and government entities routinely played important roles in the design and implementation of programs. Even so, in none of the programs was the government the primary driver behind program inception and, as a result, several programs innovatively sought and applied external resources (e.g., grants or philanthropy) in order to initiate NBS with the hope that demonstrated success would provide evidence that governments could use to rationalize investing in NBS programs. While that logic stands to reason, unfortunately none of the programs have been fully integrated widely into public health systems despite all six of the programs having achieved operational success in different ways. Furthermore, it is possible that external funding received from some programs complicated the "handover" to government agencies, even while that funding was foundational to establishing the NBS programs in the first place, a paradox that perhaps could only be avoided by confirming full government support from the outset (i.e., NBS designated as a core service and budgeted accordingly). Indeed, the longest running NBS program in Africa (Ghana) appears to have had the most substantial commitment from local government.

Another finding was the high degree of effort and dedication on the part of teams of SCD clinicians and advocates that was required to establish NBS programs. Planning routinely took a year or longer before screening started, during which time many team members worked without extra compensation and in addition to an already full workload. Therefore, progress in each of the NBS programs was all the more remarkable given the natural barriers that existed to establish them. At the same time, the achievements of each program also served to highlight how much more

work is needed given the coverage gaps resulting from high numbers of unscreened babies in each country (Figure 1). Other learnings from this study related to operational considerations (e.g., data collection and management systems) and cultural aspects (e.g., strengthening the education of community members about SCD and the rationale for screening).

Limitations of this study include the sample of programs assessed, which is less than the total number of NBS programs for SCD that have been implemented in Africa and therefore is associated with an inherent bias based on the selection of included programs. For practical reasons we surveyed a single or small number of participants from each program, and it is possible that by involving a larger cohort then additional perspectives may have been captured. Finally, it is recognized that local factors between countries, and even within countries, can influence health programs and so the lessons learned in one region will not always be immediately transferable to another. The above notwithstanding, the methodology was designed to involve a sufficiently large number of programs across different parts of the continent in order that lessons learned would be as applicable as possible across countries.

Conclusion

This study codified learnings that may be useful to help inform the design and conduct of future NBS programs for SCD in Africa. A key finding was that the capability of establishing a new program was not a guarantee that the program would endure; on the contrary some aspects of programs that were recognized enablers of their establishment (e.g., funding from external sources) may have ultimately confounded sustainability (i.e., by complicating ownership from government entities). Put another way, simply demonstrating that a program is feasible, and gathering evidence to show it is associated with positive outputs and health outcomes, may not be sufficient to garner the support needed to sustain the program in the long-term. Being aware of this scenario at the outset may help stakeholders to emphasize certain aspects of program design, including the role of government, with an aim to incorporate NBS programs into routine public health services. As such, continuing to increase awareness of the burden of SCD and the critical importance of NBS among policymakers in Africa may be a priority in order to improve the timely detection of patients and promote optimal health outcomes.

Competing Interests

NMA received clinical trial fees from Global Blood Therapeutics outside of this submitted work. VNT has served as a consultant for Novartis Pharmaceuticals, Global Blood Therapeutics, Forma Therapeutics, and Perkin Elmer. JS is an employee of the Novartis Institutes for BioMedical Research.BI received support to attend a virtual meeting from Novartis PLC and payment for educational events from Novartis PLC, Global Therapeutics. BI also participated on a data safety monitoring board/advisory board for Astrazeneca, Novartis PLC, and Global Therapeutics and was the Chair of a national hemoglobinopathy panel in England. KOF has served as a consultant for Novartis PLC.

Ethics, funding, data sharing

Ethics Statement

The Institutional Review Board of Boston Children's Hospital reviewed the study and determined that this project meets the criteria for exemption. We obtained active consent before the start of every interview.

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Data sharing statement
Background questions and the interview guide are provided in the Supplemental Materials. No additional data is available

Contributorship Statement
NMA, BI, NH, JS, and KOF planned the study, developed the interview guides, and related questions, recruited participants, reviewed the transcripts and data, wrote the initial draft of the paper, reviewed revisions including final revision. JM, SN, LT, VNT, PM, and EA shared their work with the newborn screening programs in respective countries and reviewed revisions including final revision.

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Table 1: Summary of main results

Subtheme	Core concept	Principal stakeholders	Enablers	Challenges	Examples
Theme: Program structure and governance					
Health authority endorsement	• Endorsement by government and incorporation into core health systems is fundamental to operational success and sustainability	• Governments, Ministries of Health, other local health authorities	• Government involvement from the start, in particular with plans for financial investment by national health authorities, facilitates national "ownership" of NBS programs and rational integration with routine healthcare delivery processes	• Non- or unclear involvement of government risks prioritization uncertainties, ineffective communication, and implementation challenges • Small-scale "pilot" programs can be useful for establishing proof-of-concept but may risk sustainability challenges if they do not involve buy-in from national government authorities from the outset	• In Ghana, support from Ashanti local government in is recognized to be a main factor in the program's 25+ year duration • In Angola, while the MoH was involved in the program design from the start and supported the program conceptually, financial investment to launch the program was received from a private sector partner and the motivation of MoH to fund the program long term was unclear.
Theme: Technical					
Workflow mapping	• Optimal workflows (e.g., that involve sample collection, sample transfer to laboratories, testing, patient follow-up) must be fully integrated with local health systems	• Program leaders, coordinators, health workers, laboratory staff, families	• Program design conducted in collaboration with all local stakeholders • Recognition that workflows will need to be tailored to local settings and may require iterative refinement after initial implementation	• Follow-up with patients for results notification and to enroll in comprehensive care programs is recognized as a common challenge across programs	• In Ghana, the Ghana Health Service (GHS) staff conducts most activities along the spectrum of sample collection to counseling families on results and referral for medical care; activities are integrated with the laboratory and coordinated by the dedicated staff at the Sickle Cell Foundation of Ghana
Theme: Cultural					
Community engagement	• Family participation is fundamental to screening and follow-up	• Programs leaders, coordinators, families, patient organizations and support groups	• Providing education about SCD can help families to understand the importance of NBS and following up in the event of positive screening results	• Families may not believe positive test results or fail to follow-up for routine healthcare visits since babies are asymptomatic in early infancy • SCD is stigmatized in many communities	• Newborn screening, similar to immunization was described as a "silent" public health activity that, when successful, works in the background to help keep the population healthy • Some programs described community engagement to be helpful at initiation, but specific ongoing engagement was often not necessary as long as the structures are in place for program implementation.
Theme: Funding					

Subtheme	Core concept	Principal stakeholders	Enablers	Challenges	Examples
Role of government	• NBS must be prioritized by government in order to assure long-term sustainability	• Governments, Ministries of Health, other local health authorities	• Government involvement from the start facilitates national "ownership" of NBS programs and financial planning	• Government agencies in Africa have many competing interests for spending on health	• Typically, NBS is provided free of charge to families and may be funded through a national health insurance program • In private systems, the cost of NBS is often either paid by private insurance or families • In Africa, unlike early childhood immunization, no country's government fully funds NBS programs

Table 1 summarizes the main results of the study. It is organized by the four primary themes that emerged from the analysis including governance (e.g., considerations in deploying already overcommitted clinical staff to perform NBS), technical (e.g., design and execution of operational processes), cultural (e.g., variability of knowledge and perceptions of community-based staff), and financial (e.g., issues when relying on external funding to the exclusion of government contribution). Subthemes are also highlighted as well as corresponding core concepts, stakeholders, enablers, and challenges. Examples from various country programs are also included for validity.

Table 2: Major lessons learned/recommendations

Subtheme	Lessons learned/Recommendations	Participant quotes
Theme: Program structure and governance		
Health authority endorsement	Receive endorsement by government at start of programming	• It was designed as a pilot project within the Public Health Service so that it would be incorporated. That was the plan right from the start. That it would end with government takeover was our goal. • The deputy minister of health was always a huge supporter. I would have the opportunity to meet with her whenever I wanted to, and she was always a huge supporter of the program. The Ministry wasn't able to financially support the program, but they made sure that I was able to get around stumbling blocks. And continued to do so after the study ended. • With our Ministry of Health, we have an official partnership because all the different hospitals need to have relation with the health minister. • There was some interest by the First Lady at the time, but ultimately their involvement or-- especially from the Ministry of Health side was quite low
Theme: Technical		
Workflow mapping	Integrate NBS into the local health system	• We would rely on public health nurses and doctors working in that system • The hospital director Helped to facilitate things primarily. So, we had a laboratory that we allocated within the hospital, so he helped allocate space for us to renovate a laboratory area. [This country] is one of the probably more difficult places to get either personally in and out of as a human being or to get materials in and out of. So, they helped to barter some of the supply chain stuff a little bit so that things weren't stuck in customs and people couldn't come into the country. • Whereas initially we thought once we get the funding, we thought we're going to go straight to screening. And when we went, we realized we actually had to have initial engagement with the traditional leaders and also to do some counseling work before we actually did the screening. • [One of our learnings was to] start in a place where some resources already exist (nurses, labs, etc; having a good lab in particular is crucial
Theme: Cultural		
Community engagement	Maintain interest at the Ministry of Health and hospital administration level	• There are a huge number of competing interests and everybody is overburdened and overworked and very dedicated. So, it's really easy for people to lose sight of what-- of the long-term goal of all the different projects that are going on. So, it was important to keep people's attention…at the ministry level and at the hospital administration level. • The Ministry of Health was always there to snap a photo. Unfortunately, not always there to do anything else.
Theme: Funding		
Role of government	Obtain financial commitment from government prior to the start of programming	• But we have not financial support from the government. That's the real problem in most of the African countries. It's the reason why we have foreigner partners for the financial support…. It's the reason why we can say most of our partners are foreigners • [A recurrent challenge was engagement on the Ministry of Health side.] So, for example, the people who we hired, these laboratory technicians, were supposed to be Ministry of Health employees which … being a government employee is a complicated thing. And they-- I don't even think still since-- from when we started the program until now, have had official quote unquote openings for jobs. So, they haven't hired anyone new into the system in five or six years. • There was severe engagement by the community leaders, but somehow, we could not follow that through with making the government-- so I think one of the major challenges that I would think is really the government not only engaged by accepting that is their work, but actually to get funded. So, government funding is limited. And government implementation or what they have agreed to do is significantly limited.

Table 2 summarizes the most consistent lessons learned/ recommendations highlighted across country programs for each of the primary themes. Select quotes from different respondents are included to support our recommendations. Quotes have been anonymized.

Country (approximate population size and total births): Liberia (population 5 million; 165,000 annual births)

Province or city where the program took place (approximate population size and total births): Greater Monrovia (population 1 million; 33,000 annual births)

Approximate planning period and duration of screening: 2 years planning beginning 2010; 21 months screening

Number of birth centers involved at any stage in the duration of the program: 1

Timing of screening: In the days following birth

Approximate numbers of babies screened: 3,986

Location of laboratory and laboratory screening method: Noguchi Memorial Institute for Medical Research, University of Ghana, Legon; initial screening method: testing by IEF

Main partners involved: Thrasher Research Fund; Boston Children's Hospital; John F. Kennedy Hospital, Monrovia

Status (2021): Screening paused due to Ebola epidemic and limited funding; planning to resume screening with support from ASH CONSA

Country (approximate population size and total births): Ghana (population 30 million; 870,000 annual births)

Province or city where the program took place (approximate population size and total births): Mainly Kumasi and surrounding districts (population 3.3 million; 96,000 annual births) and one site in Accra (population 2.5 million; 73,000 annual births)

Approximate planning period and duration of screening: 4 years planning beginning 1991; 25 years screening

Number of birth centers involved at any stage in the duration of the program: 39

Timing of screening: In the days following birth; if missed, then at the first well-baby visit (approximately 2-4 weeks of age)

Approximate numbers of babies screened: 523,159 as of June 30th 2020

Location of laboratory and laboratory screening method: Noguchi Memorial Institute for Medical Research, University of Ghana, Legon Accra; IEF for screening and HPLC for confirmatory testing (however, unaffordability of HPLC reagents led to testing by IEF only)

Main partners involved: Sickle Cell Foundation of Ghana; US National Institutes of Health; Ghana and Brazilian government; Pfizer (supporting NBS at Korle Bu Teaching Hospital, Accra, since 2017); ASH CONSA (supporting 37 Military and Greater Accra Regional Hospitals since Dec 2020)

Status (2021): Active; reduced funding has forced reduction in screening sites (to 6 in 2021)

Country (approximate population size and total births): Angola (population 32 million; 1.3 million annual births)

Province or city where the program took place (approximate population size and total births): Luanda Province (population 7 million; 287 annual births) and Cabinda Province (population 800,000; 33,000 annual births)

Approximate planning period and duration of screening: 1-2 years planning beginning 2011; 10 years screening

Number of birth centers involved at any stage in the duration of the program: Initially 2 large maternity hospitals in Luanda province with expansion to 22 health centers with maternity wards in Luanda and Cabinda province

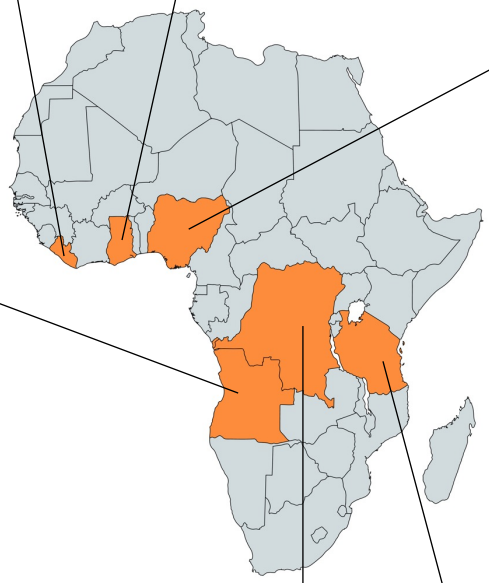
Timing of screening: In the days following birth

Approximate numbers of babies screened: 485,955

Location of laboratory and laboratory screening method: Centralized laboratory within the public pediatric hospital in Luanda utilizing IEF

Main partners involved: Texas Children's Hospital, Angola MoH, Chevron corporation

Status (2021): Paused; Chevron and Texas Children's funding/support completed in June 2020; MoH working to transition to public ownership



Country (approximate population size and total births): Nigeria (population 201 million; 7.6 million annual births)

Province or city where the program took place (approximate population size and total births): Kaduna (population 1.1. million; 42,000 annual births), Katsina (population 505,000; 19,000 annual births), and Abuja (population 1.2 million; 46,000 annual births)

Approximate planning period and duration of screening: 9 months planning beginning 2010; 18 months screening

Number of birth centers involved at any stage in the duration of the program: 4

Timing of screening: Ranged from the days following birth to 6 months of age

Approximate numbers of babies screened: 660

Location of laboratory and laboratory screening method: Abuja-Zankli Medical Centre (private hospital); HPLC (Classic model)

Main partners involved: Kafanchan and Zankli Medical Centre (Abuja), Guy's and St Thomas NHS Trust, UK; Michigan State University, US; NGO Fantsuam Foundation

Status (2021): Re-starting with EU funded project (African Research and Innovative Initiative for Sickle cell Education and ASH CONSA)

Country (approximate population size and total births): Democratic Republic of Congo (population 87 million; 3.6 million annual births)

Province or city where the program took place (approximate population size and total births): Mainly Kinshasa (population 17 million; 697,000 annual births) and also involving 3 additional provinces: Bas Congo, Kasai, Katanga (total population 14.3 million; 586,000 annual births)

Approximate planning period and duration of screening: 2 years planning beginning 2005; 14 years screening

Number of birth centers involved at any stage in the duration of the program: 262

Timing of screening: In the days following birth, in children under age 5 in tandem with an immunization program, or when newly diagnosed patients required transfusion

Approximate numbers of babies screened: Greater than 180,000 newborns and a total of more than 230.000 young children

Location of laboratory and laboratory screening method: Centre Hospitalier Monkole/Centre de Formation et d'Appui Sanitaire (CEFA) in Kinshasa and an antenna laboratory in Lubumbashi/ Katanga; IEF for screening and capillary electrophoresis for confirmatory testing

Main partners involved: Centre Hospitalier Monkole/Centre de Formation et d'Appui Sanitaire (CEFA); European Union; Agence Française de Développement (AFD), DGD Coppération Belge; Pierre Fabre Foundation; Association for Cultural, Technical, and Educational Cooperation/Belgium (ACTEC) ; Institut Européen de Coopération et de Développement/France (IECD) ; Instituto per la Cooperazione Universitaria, Italy (ICU)

Status (2021): Reduction of screening due to lack of funding

Country (approximate population size and total births): Tanzania (population 58 million; 2.1 million annual births

Province or city where the program took place (approximate population size and total births): Dar-es-Salaam (population 4.4 million; 163,000 annual births) and Mwanza (population 2.8 million; 104,000 annual births)

Approximate planning period and duration of screening: 1 year planning beginning 2015; 24 months of screening

Number of birth centers involved at any stage in the duration of the program: 3

Timing of screening: In the days following birth

Approximate numbers of babies screened: 6,000

Location of laboratory and laboratory screening method: Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania; Isoelectric focusing and HPLC

Main partners involved: Muhimbili University of Health and Allied Sciences

Status (2021): Active through research activities (Fogarty K43 Emerging Global Leader Award and the Sickle Pan-African Research Consortium) and health projects (ASH CONSA)

Supplemental Materials

I. Background questions

Questions sent by email ahead of interview and discussed at the start of each interview

a. In what city or geographic region was/is the program?

b. What is the approximate population size of the catchment area(s) covered?

c. About how long was the program planning process before screening started?

d. When did screening start?

e. Did the program end or is it ongoing?

f. If it ended, how long did it run for?

g. How babies were, or have been, screened in total?

h. How many birth centers were/are involved in the program?

II. Interview guide: Phase one

INTRODUCTION

Thank you for speaking with me today. My name is [name here]. As I mentioned in our email exchange, we are doing a study to inform success of newborn screening programs in Africa by assessing enablers and barriers to these programs by learning from the experiences of programs that had been established in the past and programs that are ongoing.

Over the next few months we aim to speak with representatives from various programs. Our plan is to distill the learnings into a format that can be used practically by various stakeholders including health workers, policy makers, NGOs, and others. We anticipate a publication, which we would invite you to review and take part in.

Note that this project received Institutional Review Board (IRB) exemption from the Boston Children's Hospital. We won't be asking for any patient information.

Today, I'd like to learn about your experience with the SCD newborn screening program in [country]. By agreeing to this interview, it is understood that you are in a position to comment on the newborn screening program that took place there and have the necessary authorization to speak on behalf of the program.

Would it be ok for me to audio-record the interview? That will help be sure we don't miss anything when we do the analyses. In the write-up, we won't attribute any specific statements to you unless we get your permission for that.

Any questions or comments?

Thank you so much again. Ok—let's get started with the interview, which will take about 45 minutes.

INTERVIEW

1. Email survey questions

If any email survey questions not answered or need clarification—ask those first. If all have been answered, then move on to next section.

2. Partners

- Who were all the partners involved in the program?
  [Govt, MOH, University, teaching hospital, NGO, professional societies, consultants, other]
  [Categorize: local partner vs international partner]

- Which partner or partners would you say had the biggest role in planning the program? Can you describe their role?

- Which partner or partners would you say had the biggest role in running the program? Can you describe their role?

- What were the main roles of the other partners?
  [Ask specifically about role of government/MOH]

- What was it like to get buy-in from the other partners? What was your approach? Could you tell me more?

3. Planning

- How did the idea for the program come about in the first place?

- What was helped the program most in the planning phase?

- What was the biggest challenge you faced in the planning phase?

- Was it envisioned at the start as a "pilot" program with a defined endpoint? Could you tell me more about that?

4. Launch

- Was there some sort of launch event when screening started?

- If so, was that important? What did the launch event consist of? Could you tell me more about that?

5. Logistics

- Who managed the day-to-day operation of the program?
  [Profile of managers (nurse, doctor, etc), team composition (how many), full-time/part-time]

- Was there a "headquarters" for the newborn screening program? If so, where was it located?

- Could you describe the birth centers where newborn screening took place?
  [Clinics, hospital, urban, rural]

- Were babies screened before leaving facility, or did they return for screening at a later date? How do you think this affected the success of the program?

- Who did most of the heelsticks? About how many participated in the program?
  [Want to learn how many nurses and/or other health workers were trained/participated in the program in the various birth centers where screening took place]

- Was there a consent process for families before obtaining heelstick? If so, could you please describe it?

- Could you briefly describe the sample collection and transport process from the point of heelstick to the screening laboratory? Were there any major problems in handling the samples?

- *How did patient information get to the screening lab? How did results get back to patients?* Did you use a specific computer program to manage information—if so, which one? Were there any major problems in collecting or managing data/information?

- What in your opinion were the most important factors that led to success in day-to-day operation of the program?

- What were the biggest challenges in day-to-day operation of the program?

- Were modifications to the way the program ran made over time?

6. Laboratory

- Was a SCD screening lab newly set up in conjunction with the screening program, or was an already established SCD screening lab used? Was the lab located in the same facility where screening occurred? How did that affect success?

- Who worked in the laboratory to analyze the samples?
[Profile of staff (techs, etc), team composition (how many), full-time/part-time]

- Did the lab have equipment problems? Staffing problems? Could you tell me more? [*How did this affect how the lab ran?]*

- What method was used to conduct the screening test?
[For example, isoelectric focusing]

- Do you happen to know what specific equipment was used in the lab?
[E.g., brand name of isoelectric focusing machine]

- What was the most important factor in the successful running of the lab?

- What was the biggest barrier to running the lab?

7. Notification and follow-up

- If a baby screened positive, how were the parents notified? Who did that communication? What messages were delivered?

- What was the process for babies that screened positive—for example, did they get enrolled in a clinical management program? Could you tell me more about that? *[Seeking details of the sickle cell management program, if there was one]*

8. Funding

- How was the program funded? Were the costs shared by different parties

- What were/are the parts of the program that are most expensive?

- Would you be comfortable sharing the approximate cost of the program?
[Start-up costs, annual running costs]

- How did costs affect the program? *[were activities, services, scale, sustainability etc. affected for financial reasons?]*

9. Program disposition

- **If the program has ended**—did it end when planned, go for longer than planned, or end prematurely? What do you think were the main reasons for this?

- **If the program is ongoing**—has it remained stable size, grown, or diminished in size? What do you think have been the main reasons for this?

10, Perceptions

- How did you and the other leaders of this program define [and measure] success?

- Could you comment on how families viewed the program? Could you tell me more about that? [*if viewed negatively, how did the program deal with that?]*

- What was your own biggest learning in doing this program?

11. Closing

- Are there any reports or publications about the program that could be shared with me?

- Is there anything else that you think I should know that we didn't talk about?

- Based on the interviews, we'll be writing a report summarizing the findings and we would like to acknowledge your contribution. Is that ok? We will share the report with you when it's ready and it would be great to get your feedback.

- In addition to you, we have also spoken with Dr. [name] from [country, Dr [name] from [country], etc. Are you aware of other newborn screening programs in Africa and contacts that we haven't yet connected with?

Thank you very much for speaking with me.

Bye!

III. Main topic categories for phase two interviews

For each, discussing how it impacted success, challenges, enablers, and other lessons learned.

- Cultural issues (among providers and community)
- Sustainability
- Balance of involvement between external and local partners
- Notification and follow up

IV. Interview guide: Phase two

INTRODUCTION

Thank you for speaking with me today. My name is Natalie. As I mentioned in our email exchange, we are doing a study to inform success of NBS programs in Africa by assessing enablers and barriers to these programs by learning from the experiences of programs that had been established in the past and programs that are ongoing.

Over the next few months we aim to speak with representatives from various programs. Our plan is to distill the learnings into a format that can be used practically by various stakeholders including health workers, policy makers, NGOs, and others. We anticipate a publication, which we would invite you to review.

Note that this project received Institutional Review Board (IRB) exemption from the Boston Children's Hospital. We won't be asking for any patient information.

Today, I'd like to learn about your experience with the SCD newborn screening program in [country]. By agreeing to this interview, it is understood that you are in a position to comment on the NBS program that took place there and have the necessary authorisation to speak on behalf of the program.

Would it be ok for me to audio-record the interview? That will help be sure we don't miss anything when we do the analyses. In the write-up, we won't attribute any specific statements to you unless we get your permission for that.

Any questions or comments?

Thank you so much again. Ok—let's get started with the interview, which will take about 45 minutes.

INTERVIEW

1. Email survey questions

If any email survey questions not answered or need clarification—ask those first. If all have been answered, then move on to next section.

2. Partners

Who were the partners involved in the program?

- What was the role of local leaders and champions in the program?
- What was the role of external partners?
- What was the role of the government?

- How did they affect the success of the program?
- What lessons learned or recommendations do you have about working with partners?

3. Logistics

- Can you please walk me through the entire screening process for one baby starting with how the baby is identified through how the parents are notified?
    - Probes: data management systems, equipment and supplies needed, getting results back to patients

- What in your opinion were the most important factors that led to success in day-to-day operation of the program?

- What were the biggest challenges in day-to-day operation of the program?

- What lessons learned or recommendations do you have about running the day to day operations of the program?

- Probe: challenges and facilitators for running the lab, recommendations

4. Program disposition

- **If the program has ended**—did it end when planned, go for longer than planned, or end prematurely? What do you think were the main reasons for this?
    - What would be needed in order to have a sustainable program?

- **If the program is ongoing**—has it remained stable size, grown, or diminished in size? What do you think have been the main reasons for this?

- Who pays for it?

- What recommendations do you have for other programs in the planning and implementation phase that can set them up to be sustainable?

5. Perceptions

- Could you comment on how families and the community viewed the program? Could you tell me more about that? [*if viewed negatively, how did the program deal with that?]*
    - *Probes: stigma, need for education*

- How did this impact the success of the program?

- What was your own biggest learning from the program?

6. Closing

- Are there any reports or publications about the program that could be shared with me?

- Is there anything else that you think I should know that we didn't talk about?

- Based on the interviews, we'll be writing a report summarizing the findings and we would like to acknowledge your contribution. Is that ok? We will share the report with you when it's ready and it would be great to get your feedback.

Thank you very much for speaking with me.

Bye!

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Enablers and barriers to newborn screening for sickle cell disease in Africa: results from a qualitative study involving programs in six countries

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Title: Enablers and barriers to newborn screening for sickle cell disease in Africa: results from a qualitative study involving programs in six countries

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Abstract

Objectives: Given the fundamental role of newborn bloodspot screening (NBS) to enable prompt diagnosis and optimal clinical management of individuals with sickle cell disease (SCD), we sought to systematically assess enablers and barriers to implementation of NBS programs for SCD in Africa using established qualitative research methods.

Setting: Childbirth centers and NBS laboratories from 6 countries in East, West, and Southern Africa.

Participants: Eight program leaders involved with establishing and operating NBS programs for SCD in Angola, Democratic Republic of Congo, Ghana, Liberia, Nigeria, and Tanzania.

Primary and Secondary Outcome Measures: Data obtained through a structured, phased interview approach were analyzed using a combination of inductive and deductive codes and used to determine primary themes related to the implementation and sustainability of SCD NBS programs.

Results: Four primary themes emerged from the analysis relating to governance (e.g., pragmatic considerations when deploying overcommitted clinical staff to perform NBS), technical (e.g., design and execution of operational processes), cultural (e.g., variability of knowledge and perceptions of community-based staff), and financial (e.g., issues that can arise when external funding may effectively preclude government inputs) aspects. Key learnings included perceived factors that contribute to long-term NBS program sustainability.

Conclusions: The establishment of enduring NBS programs is a proven approach to improving the health of populations with SCD. Organizing such programs in Africa is feasible but initial implementation does not assure sustainability. Our analysis suggests that future programs should prioritize government partner participation and funding from the earliest stages of program development.

Article Summary

Strengths and limitations of this study

Strengths

- This is one of the largest studies of enablers and barriers to successful implementation and sustainability of sickle cell disease newborn screening programs in Africa, where no national-level programs currently exist.
- Applying established qualitative research methods, this study investigated the firsthand experiences of clinical and coordinating leaders involved in establishing and operating programs in six African countries: Angola, Democratic Republic of Congo, Ghana, Liberia, Nigeria, and Tanzania.

Limitations

- Six programs were included in the analysis, which is a sample of the total number of newborn screening programs for sickle cell disease that have been implemented in Africa
- By design, a single or small number of participants were surveyed from each program
- The lessons learned from one country may not always be immediately transferable to other countries due to various local factors.

Introduction

Sickle cell disease (SCD) is one of the world's commonest hemoglobinopathies, estimated to affect in excess of 400,000 newborns annually with 80% of patients born into populations living in low and middle-income countries.[1,2] The disease is caused by a single point mutation in the beta-globin gene that results in the formation of sickle hemoglobin (hemoglobin S, or HbS).[3] Under certain conditions including hypoxia, HbS polymerizes and creates distorted (i.e., "sickle"-shaped), adherent, and less deformable red blood cells (RBCs).[4] The result is easily-hemolyzed RBCs with a shortened lifespan, endothelial damage, vessel obstruction, and other pathophysiological effects that collectively contribute to the development of a vast constellation of acute and chronic clinical manifestations and, often, premature mortality.

Fetal hemoglobin (HbF), the predominant hemoglobin during gestation and in neonates, is the most potent known inhibitor of HbS polymerization. As such, infants with SCD are asymptomatic until HbF levels decline to low levels, typically within the first 6-24 months of life. Early diagnosis prior to the predominance of HbS is critical to allow for provision of early lifesaving interventions. Since SCD cannot be diagnosed by clinical signs at birth, newborn bloodspot screening (NBS) materialized decades ago to be a standard approach in many high-resource countries for identifying babies with SCD before complications develop.[5,6] Early detection enables the prompt initiation of parental education and evidence-based preventative care practices that include penicillin prophylaxis and pneumococcal vaccination.[7,8]

In the 1980s, a randomized, placebo-controlled trial in the United States confirmed the efficacy of penicillin prophylaxis in significantly reducing incidence of and mortality due to *Streptococcus pneumoniae*, the leading cause of death in young children with SCD.[5] Evidence from that study provided the impetus for the U.S. National Institutes of Health Consensus Development Conference on Newborn Screening for SCD and Other Hemoglobinopathies to recommend that all babies born in the United States be screened for SCD.[9] In the United States, where universal NBS for SCD (i.e., testing newborn babies within the first few weeks after birth) has existed in all 50 states since 2006, NBS is largely acknowledged to be among the most important factors leading to high rates (well over 90%) of survival into adulthood.[5,10,11] Universal screening for SCD now constitutes national policy in the United States, Brazil, United Kingdom, Germany, Spain, Netherlands, and Malta;[12–15] longstanding NBS programs have also been in place in other parts of Europe, Jamaica, Ghana and Canada.[13,16,17] Targeted screening of newborns (e.g., according to ancestry), is implemented in some regions but has been shown to be less effective compared with universal screening at identifying infants with disease and preventing deaths.[18]

The vast majority of people with SCD globally are born in Africa where up to 2% or more of births are reported to be affected in some regions, contributing silently but significantly (8-16%) to under 5 mortality in high burden countries.[19–21] While no country in Africa has yet implemented policies for universal screening, various national NBS programs for SCD have been organized, and with heightened awareness about the impact of the disease there is optimism for increased progress in the future.[19,20,22–26] In this context we sought to characterize the enablers and challenges to conducting NBS for SCD based on the experiences of previous and ongoing programs. Specifically, we assessed programs in Angola, Democratic Republic of Congo (DRC), Ghana, Liberia, Nigeria, and Tanzania.[19,20,23–25,27] Using established qualitative research methods,[28–30] we conducted semi-structured interviews with clinical and coordinating leaders involved in each program and extracted key messages to codify main lessons learned. This analysis is envisioned to be a resource for patients, clinicians, policymakers, and other stakeholders seeking to improve health systems relating to NBS for SCD in Africa and other limited resource settings globally where SCD occurs in high prevalence.

Methods

Study design

We conducted a qualitative descriptive study that incorporated data from semi-structured interviews with individuals who were responsible for, or significantly involved in, the design and implementation of NBS programs for SCD in an African country (hereafter referred to as "participants").[31] The purpose of the interviews was to describe the process for designing and implementing the programs, identify enablers and challenges, and elicit lessons learned in order to facilitate a concise summary of learnings that could be used to inform future SCD NBS programs. Additionally, participants provided background information about their program by email in advance of their interview. If a participant did not provide the information prior to their interview, then these questions were asked at the start of the interview. See Supplemental Materials for the background questions and interview guide.

Interviews were conducted in two phases. The first phase included four participants (representing programs in Ghana, Angola, DRC, and Liberia), who answered a comprehensive set of questions about their programs. Interviews were transcribed, coded and analyzed after the first phase of data collection. From this analysis, the study team identified aspects of SCD NBS program that warranted deeper exploration either because they emerged as critical to the success of the program or because they were characterized by variability that prompted deeper investigation across programs. The latter included aspects of the program that were subjective (e.g., cultural attitudes towards SCD) as opposed to mechanistic (e.g., the type of test used to screen for SCD). The second phase included 2 participants (representing programs in Nigeria and Tanzania) who answered questions on the topics determined in phase 1 that required further discussion. By limiting the number of questions asked in the second phase, the study team was able to conduct deeper exploration of each of the topics. The findings from phase two supplemented the results from the corresponding topics in phase 1. The results from the two phases were analyzed together to identify key learnings for the establishment and maintenance of SCD NBS programs in Africa.

Patient and participant involvement

Patients were not involved in this study. Participants were identified by study members as program leaders after reviewing publications related to SCD NBS in African countries. Participants were recruited by email. During the recruitment, all participants confirmed that they were program leaders and they reported various levels of public engagement in their respective countries. All participants were invited to review the results and to contribute to identifying key messages and implications of the results, clarify or correct any information from their interviews, and co-author the resulting manuscript (i.e., in alignment with a form of "member checking" described in the literature).[32] One participant was also a study member (KOF). This study member was not involved in the coding, analysis or preliminary interpretations of the data to minimize the risk that this study member's own experiences would bias the results.

Interview guide

We designed the interview guide to gain insight into how participants developed, implemented and, when applicable, sustained their program. The team's qualitative researcher (NH) led the creation of the interview guide with input from a study team member with extensive knowledge about SCD newborn screening programs in Africa (KOF) and from study team members with general expertise about SCD (JS, NA). Collectively, the study team identified the key steps of establishing and implementing a screening program as well as other factors that were likely to impact the success of the program. These high-level topics included: program partners, planning the program, launching the program, logistics of day-to-day operations, establishing and running

the laboratory, patient notification and follow-up, funding and costs, program disposition, and perceptions of the program by families of newborns. The interview guide was piloted with a member of the study team (KOF) for clarity, flow, and duration. Minor revisions to the interview guide were made based on his feedback and his responses were included in the dataset.

Data collection and analysis

Participants were interviewed one time for approximately 1 hour. Phase one interviews took place between October and December 2017. Phase two interviews took place between July and September 2019. All interviews were conducted by phone, audio recorded, and transcribed verbatim. Phase 1 interviews were conducted by the qualitative specialist on the team (NH) who received training on SCD-specific content from the other team members and studied relevant literature to become additionally familiar with the topic. Phase 2 interviews were conducted by a team member with content expertise who had prior interviewing experience (JS).

We performed a thematic analysis of the interviews using a coding scheme developed with a combination of inductive and deductive codes. In phase one, coding was performed in NVivo (QSR) and the content from each code was summarized in a table, including key quotes and identification of key findings. Key findings were used to identify areas that required more in-depth exploration during the second phase of data collection. Phase two interviews were analyzed by directly adding key findings into the summary tables from Phase one. Results were shared with the participants for feedback and, if needed, corrections, clarifications, and the addition of missing information.

Ethics

The Institutional Review Board of Boston Children's Hospital reviewed the study and determined that this project meets the criteria for exemption. We obtained active consent before the start of every interview.

Results

Study sample

The study involved data collection relating to NBS programs in six countries in Africa (Figure 1) with representation from West (Ghana, Liberia, Nigeria), Central (Angola, Democratic Republic of Congo), and East Africa (Tanzania). Participants were based at academic institutions and professional societies; many had worked in conjunction with government agencies and external collaborators. The planning period before the initiation of screening ranged from approximately 9 months to 4 years, and the duration of screening ranged from 21 months to 25 years. The number of birth centers involved in the NBS programs ranged from one to approximately 250. Most programs are ongoing in some capacity, albeit several with reported periods of inactivity due to various operational challenges as described below.

Qualitative findings

Four primary themes emerged in the analysis relating to (a) structure and governance; (b) technical aspects; (c) culture; and (d) finances. Within these four main themes we identified 12 sub-themes that are summarized in Table 1 and described below. A summary of major lessons learned/recommendations is provided in Table 2.

Primary theme I: Structural and governance aspects

The role of national health authorities was universally felt to be a critical determinant of success. Government entities, including Ministries of Health and/or other national health service delivery units, were involved in each of the programs with a level of engagement that ranged along a

continuum from passive (e.g., conceptual "support" of the program and allowance to proceed without allocating new resources) to active (e.g., recognizing the NBS program as a core part of the health system and providing clinical staff and other resources to maintain its continuity). While in several countries the government was involved from the early stages of NBS program design, in no country was the government the initial actor involved in establishing the NBS program. Programs that continued beyond a "pilot" phase ascribed government involvement as a key enabler; likewise, programs that met with challenges in achieving long-term sustainability pointed to lack of government ownership as a main reason.

All participants reported the topic of program structure and governance to be an essential consideration. Programs were each championed by clinician-led teams with specialized expertise in caring for patients with SCD. All programs focused mainly on births taking place in public health (i.e., government-operated) facilities; private sector birth centers were less commonly included. Clinical and ancillary staff (e.g., midwives and nurses) that worked at birth centers and were responsible for the hands-on aspects of screening (i.e., conducting heelsticks, communicating with families, etc.) were generally government-employed workers who had been on staff prior to the initiation of the NBS program. In most cases, therefore, the work associated with NBS constituted a new task they were asked to perform in addition to other duties. Across the programs, coordinating staff played a fundamental role in organizing and overseeing a vast array of logistics and managing the relationships with multiple stakeholders that variably included families, birth center staff, SCD clinical experts, government representatives, and external collaborators including clinician colleagues and funding partners.

An important sub-theme relating to staffing concerned the availability of specialized clinical "Centers of Excellence" that would be capable of providing holistic preventative and treatment services for individuals that were diagnosed with SCD through the NBS programs. Participants recognized that the existence of such centers, and their accessibility to patients, was a pre-requisite to the initiation of NBS programs such that families could be immediately offered a clinical service for follow-up upon notification of positive test results.

Primary theme II: Technical aspects

While the general workflows involved in NBS programs are conceptually straightforward (e.g., sample acquisition, laboratory testing, and notification of results), the design and execution of consistent operational processes was reported by several programs to be an intensive and challenging exercise in practice. This was felt in part to be due to the very high level of coordination that was required between practitioners at birthing sites (who were responsible for collecting specimens, organizing specimen transport to the laboratory, receiving laboratory results, and notifying families), technicians in laboratories (who were responsible for receiving and testing specimens, and reporting laboratory results), and coordinators that oversaw NBS programs (responsible for ensuring adequate training of staff, reliable availability of equipment and supplies, reporting to national authorities, and other activities). In one program the laboratory was located in a different city from the birth centers, requiring the specimens to be transported by an approximately 7-hour car ride from the birthing sites to the laboratory. Another program shipped specimens in a sealed container at 4^{o}C by plane to the NBS program laboratory in another country. The ambition of most programs was to fully integrate the NBS workflows into routine health system processes; ultimately, this was achieved to a variable degree by different programs. All programs had a common aim to keep the cycle duration (i.e., from the time of specimen acquisition to the time when families were notified of results) as short as possible. One commonly cited reason for delays in the NBS workflow was tracking down families to share laboratory results—some families were not able to be contacted by phone, which necessitated in-person visits that were time consuming for NBS staff and not always successful.

Robust data collection and management systems were important to support workflows (i.e., registering babies that underwent testing, storing laboratory results, and keeping record of when families were notified of results), facilitate quality improvement of NBS programs (i.e., as a means to identify when the workflows were operating sub-optimally), and generate evidence that could be used for advocacy, research, or to inform health policy (e.g., incidence data, cost-effectiveness, or impact on health outcomes). Most programs utilized a hybrid model that involved some paper-based record keeping and some digital components. One of the programs (Ghana) converted entirely to a digital "app"-based system beginning in 2018 accessible on the phones of birth attendants, laboratory technicians, and program coordinators.

All programs, except Nigeria (where high-performance liquid chromatography (HPLC was used)), used isoelectric focusing (IEF) as the primary technique for screening or diagnosis, and some programs used HPLC or capillary electrophoresis for confirmatory testing after screening. While none of the programs surveyed reported that NBS laboratory equipment was a main barrier, virtually all of the programs reported challenges with maintaining regular maintenance of equipment or reliable access to reagents. In some cases, periodic unavailability of reagents led to delays in testing.

Primary theme III: Cultural aspects

Some NBS programs reported quick adoption of new technical practices by staff (e.g., conducting heelsticks and managing blood spot specimens) whereas other programs met with some challenges in fully integrating this practice due to the perception of increased workload. Some programs described clinical staff "champions" who became highly dedicated to the program (in the same way that many of the participants were), helped to advocate for the program, and trained other staff members. Ultimately, most programs reported achieving a state of cultural adaptation resulting in a sense of pride amongst the program staff for being involved in a novel program with profound implications for the health of individuals with SCD.

Community engagement was highlighted by several programs as an important determinant of success. It was reported that knowledge about SCD amongst community members varied widely and was occasionally confounded by false perceptions about the disease or stigmatization. In some cases, the cultural aspects of community engagement were noted to be a determinant in the ability of NBS program staff to follow-up with families to provide notification of test results (i.e., if families were fearful of receiving results). Participants noted that families could also be dubious of positive results in the face of a baby who is healthy appearing (since babies with SCD are universally asymptomatic in early infancy).

Primary theme IV: Financial aspects

In all programs NBS services were provided free of charge to families. Participants reported an idealized scenario where NBS programs were entirely funded by local or national governments such that programs were fully integrated as part of routine public health services.

Several program leaders raised the idea of cost-sharing between NBS programs as a potential approach for reducing the costs borne by each individual program. One example that was implemented was the shipping of laboratory specimens from one country to another for testing. Another example that was raised as a concept but not yet implemented was purchasing materials such as reagents for laboratory equipment in bulk.

All programs received some form of external funding, defined as funding from out-of-country entities. Sources of external funding included foundations, non-governmental organizations,

private sector companies, and governments of other countries. Many participants reported external funding to have been an important enabler in helping to establish and/or maintain operations, and in some cases the cessation of external funding resulted in the need to scale down or halt the program. External funding was therefore generally perceived to be a "double-edge sword" whereby it had been necessary for some programs to manifest but at the same time it complicated the attainment of long-term sustainability since permanent funding from outside sources was not feasible.

Discussion

Newborn screening programs constitute a standard approach for diagnosing SCD in several countries and are urgently needed in Africa to assure that affected individuals promptly receive essential counseling as well as preventative and therapeutic care.[2,33] The reality, however, is that the establishment and sustained operation of NBS programs in Africa is complex due to many factors. In an effort to better understand experience-based and pragmatic determinants of success, this study sought to harness lessons learned from participants involved in establishing and operating NBS programs that took place across West, Central, and East Africa. While there are numerous published reports of progress achieved with sub-national NBS programs for SCD in individual countries,[19,20,23–25] we had identified only a single previous report that analyzed cross-country experiences; that study described pilot programs in DRC and Burkina Faso and presented an excellent review of the rationale for SCD NBS programs along with high-level guidance for selected aspects of their implementation.[34] Thus, to our knowledge, the current study involving programs in six countries constitutes the first attempt to integrate learnings from a "critical mass" of NBS programs for SCD in Africa. Through standard qualitative methods, four main themes encompassing twelve sub-themes emerged that highlight enablers and barriers to implementation.

A main and crucial finding of this study was confirmation that NBS programs for SCD are feasible to successfully implement in Africa, as evidenced by the large numbers of babies screened (e.g., tens of thousands) and the long duration of screening (e.g., more than 25 years) that was demonstrated in some programs. Nevertheless, a consistent narrative emerged that feasibility did not ensure sustainability. Many of the programs reported periodic setbacks in their capabilities to maintain their planned level of operations or to expand, and some programs were forced to cease operations. In no case were technical or workflow issues the primary challenge; rather, there was general consensus that the greatest barrier to the long-term success of NBS programs resulted from their incomplete adoption into routine health systems. This was attributed mostly to inter-related aspects of governance (in particular, government involvement) and funding.

Government commitment was recognized by all interviewees as an essential element of success, and government entities routinely played important roles in the design and implementation of programs. Even so, in none of the programs was the government the primary driver behind program inception and, as a result, several programs innovatively sought and applied external resources (e.g., grants or philanthropy) in order to initiate NBS with the hope that demonstrated success would provide evidence that governments could use to rationalize investing in NBS programs. While that logic stands to reason, unfortunately none of the programs have been fully integrated widely into public health systems despite all six of the programs having achieved operational success in different ways. Furthermore, it is possible that external funding received from some programs complicated the "handover" to government agencies, even while that funding was foundational to establishing the NBS programs in the first place, a paradox that perhaps could only be avoided by confirming full government support from the outset (i.e., NBS designated as a

core service and budgeted accordingly). Indeed, the longest running NBS program in Africa (Ghana) appears to have had the most substantial commitment from local government.

Another finding was the high degree of effort and dedication on the part of teams of SCD clinicians and advocates that was required to establish NBS programs. Planning routinely took a year or longer before screening started, during which time many team members worked without extra compensation and in addition to an already full workload. Therefore, progress in each of the NBS programs was all the more remarkable given the natural barriers that existed to establish them. At the same time, the achievements of each program also served to highlight how much more work is needed given the coverage gaps resulting from high numbers of unscreened babies in each country (Figure 1). Other learnings from this study related to operational considerations (e.g., data collection and management systems) and cultural aspects (e.g., strengthening the education of community members about SCD and the rationale for screening).

Limitations of this study include the sample of programs assessed, which is less than the total number of NBS programs for SCD that have been implemented in Africa and therefore is associated with an inherent bias based on the selection of included programs. For practical reasons we surveyed a single or small number of participants from each program, and it is possible that by involving a larger cohort then additional perspectives may have been captured. Finally, it is recognized that local factors between countries, and even within countries, can influence health programs and so the lessons learned in one region will not always be immediately transferable to another. The above notwithstanding, the methodology was designed to involve a sufficiently large number of programs across different parts of the continent in order that lessons learned would be as applicable as possible across countries.

Conclusion

This study codified learnings that may be useful to help inform the design and conduct of future NBS programs for SCD in Africa. A key finding was that the capability of establishing a new program was not a guarantee that the program would endure; on the contrary some aspects of programs that were recognized enablers of their establishment (e.g., funding from external sources) may have ultimately confounded sustainability (i.e., by complicating ownership from government entities). Put another way, simply demonstrating that a program is feasible, and gathering evidence to show it is associated with positive outputs and health outcomes, may not be sufficient to garner the support needed to sustain the program in the long-term. Being aware of this scenario at the outset may help stakeholders to emphasize certain aspects of program design, including the role of government, with an aim to incorporate NBS programs into routine public health services. As such, continuing to increase awareness of the burden of SCD and the critical importance of NBS among policymakers in Africa may be a priority in order to improve the timely detection of patients and promote optimal health outcomes.

Figure 1: Location and characteristics of included programs. Program data provided by country participant(s) who were interviewed. Abbreviations: ASH (American Society of Hematology), CONSA (Consortium on Newborn Screening in Africa), isoelectric focusing (IEF), high-performance liquid chromatography (HPLC), Ministry of Health (MoH), United States (US), United Kingdom (UK), Non-governmental organization (NGO) National Health Services (NHS). Reference for demographic data: World Bank. Map design credit: Mapchart.net.

Competing Interests

NMA received clinical trial fees from Global Blood Therapeutics outside of this submitted work. VNT has served as a consultant for Novartis Pharmaceuticals, Global Blood Therapeutics, Forma Therapeutics, and Perkin Elmer. JS is an employee of the Novartis Institutes for BioMedical Research.BI received support to attend a virtual meeting from Novartis PLC and payment for educational events from Novartis PLC, Global Blood Therapeutics. BI also participated on a data safety monitoring board/advisory board for Astrazeneca, Novartis PLC, and Global Blood Therapeutics and was the Chair of a national hemoglobinopathy panel in England. KOF has served as a consultant for Novartis PLC.

Ethics, funding, data sharing

Ethics Statement

Boston Children's Hospital Institutional Review Board

(IRB-P00025918)

The Institutional Review Board (IRB) reviewed the above referenced protocol and determined that it qualifies as exempt from the requirements of 45 CFR 46.

This protocol was determined to be exempt because it is limited to research activities in which the only involvement of human subjects will be in the following category/ies described in 45 CFR 46.101.(b):

(1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

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Data sharing statement

Not applicable as background questions and the interview guide are provided in the Supplemental Materials.

Contributorship Statement

NMA, BI, NH, JS, and KOF planned the study, developed the interview guides, and related questions, recruited participants, reviewed revisions including final revision. NMA, BI, NH, and JS reviewed the transcripts and data and wrote the initial draft of the paper. JM, SN, LT, VNT, PM, and EA shared their work with the newborn screening programs in respective countries and reviewed revisions including final revision.

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Table 1: Summary of main results

Subtheme	Core concept	Principal stakeholders	Enablers	Challenges	Examples
Theme: Program structure and governance					
Health authority endorsement	• Endorsement by government and incorporation into core health systems is fundamental to operational success and sustainability	• Governments, Ministries of Health, other local health authorities	• Government involvement from the start, in particular with plans for financial investment by national health authorities, facilitates national "ownership" of NBS programs and rational integration with routine healthcare delivery processes	• Non- or unclear involvement of government risks prioritization uncertainties, ineffective communication, and implementation challenges • Small-scale "pilot" programs can be useful for establishing proof-of-concept but may risk sustainability challenges if they do not involve buy-in from national government authorities from the outset	• In Ghana, support from Ashanti local government in is recognized to be a main factor in the program's 25+ year duration • In Angola, while the MoH was involved in the program design from the start and supported the program conceptually, financial investment to launch the program was received from a private sector partner and the motivation of MoH to fund the program long term was unclear.
Theme: Technical					
Workflow mapping	• Optimal workflows (e.g., that involve sample collection, sample transfer to laboratories, testing, patient follow-up) must be fully integrated with local health systems	• Program leaders, coordinators, health workers, laboratory staff, families	• Program design conducted in collaboration with all local stakeholders • Recognition that workflows will need to be tailored to local settings and may require iterative refinement after initial implementation	• Follow-up with patients for results notification and to enroll in comprehensive care programs is recognized as a common challenge across programs	• In Ghana, the Ghana Health Service (GHS) staff conducts most activities along the spectrum of sample collection to counseling families on results and referral for medical care; activities are integrated with the laboratory and coordinated by the dedicated staff at the Sickle Cell Foundation of Ghana
Theme: Cultural					
Community engagement	• Family participation is fundamental to screening and follow-up	• Programs leaders, coordinators, families, patient organizations and support groups	• Providing education about SCD can help families to understand the importance of NBS and following up in the event of positive screening results	• Families may not believe positive test results or fail to follow-up for routine healthcare visits since babies are asymptomatic in early infancy • SCD is stigmatized in many communities	• Newborn screening, similar to immunization was described as a "silent" public health activity that, when successful, works in the background to help keep the population healthy • Some programs described community engagement to be helpful at initiation, but specific ongoing engagement was often not necessary as long as the structures are in place for program implementation.
Theme: Funding					

Subtheme	Core concept	Principal stakeholders	Enablers	Challenges	Examples
Role of government	• NBS must be prioritized by government in order to assure long-term sustainability	• Governments, Ministries of Health, other local health authorities	• Government involvement from the start facilitates national "ownership" of NBS programs and financial planning	• Government agencies in Africa have many competing interests for spending on health	• Typically, NBS is provided free of charge to families and may be funded through a national health insurance program • In private systems, the cost of NBS is often either paid by private insurance or families • In Africa, unlike early childhood immunization, no country's government fully funds NBS programs

Table 1 summarizes the main results of the study. It is organized by the four primary themes that emerged from the analysis including governance (e.g., considerations in deploying already overcommitted clinical staff to perform NBS), technical (e.g., design and execution of operational processes), cultural (e.g., variability of knowledge and perceptions of community-based staff), and financial (e.g., issues when relying on external funding to the exclusion of government contribution). Subthemes are also highlighted as well as corresponding core concepts, stakeholders, enablers, and challenges. Examples from various country programs are also included for validity.

Table 2: Major lessons learned/recommendations

Subtheme	Lessons learned/Recommendations	Participant quotes
Theme: Program structure and governance		
Health authority endorsement	Receive endorsement by government at start of programming	• It was designed as a pilot project within the Public Health Service so that it would be incorporated. That was the plan right from the start. That it would end with government takeover was our goal. • The deputy minister of health was always a huge supporter. I would have the opportunity to meet with her whenever I wanted to, and she was always a huge supporter of the program. The Ministry wasn't able to financially support the program, but they made sure that I was able to get around stumbling blocks. And continued to do so after the study ended. • With our Ministry of Health, we have an official partnership because all the different hospitals need to have relation with the health minister. • There was some interest by the First Lady at the time, but ultimately their involvement or-- especially from the Ministry of Health side was quite low
Theme: Technical		
Workflow mapping	Integrate NBS into the local health system	• We would rely on public health nurses and doctors working in that system • The hospital director Helped to facilitate things primarily. So, we had a laboratory that we allocated within the hospital, so he helped allocate space for us to renovate a laboratory area. [This country] is one of the probably more difficult places to get either personally in and out of as a human being or to get materials in and out of. So, they helped to barter some of the supply chain stuff a little bit so that things weren't stuck in customs and people couldn't come into the country. • Whereas initially we thought once we get the funding, we thought we're going to go straight to screening. And when we went, we realized we actually had to have initial engagement with the traditional leaders and also to do some counseling work before we actually did the screening. • [One of our learnings was to] start in a place where some resources already exist (nurses, labs, etc; having a good lab in particular is crucial
Theme: Cultural		
Community engagement	Maintain interest at the Ministry of Health and hospital administration level	• There are a huge number of competing interests and everybody is overburdened and overworked and very dedicated. So, it's really easy for people to lose sight of what-- of the long-term goal of all the different projects that are going on. So, it was important to keep people's attention…at the ministry level and at the hospital administration level. • The Ministry of Health was always there to snap a photo. Unfortunately, not always there to do anything else.
Theme: Funding		
Role of government	Obtain financial commitment from government prior to the start of programming	• But we have not financial support from the government. That's the real problem in most of the African countries. It's the reason why we have foreigner partners for the financial support…. It's the reason why we can say most of our partners are foreigners • [A recurrent challenge was engagement on the Ministry of Health side.] So, for example, the people who we hired, these laboratory technicians, were supposed to be Ministry of Health employees which … being a government employee is a complicated thing. And they-- I don't even think still since-- from when we started the program until now, have had official quote unquote openings for jobs. So, they haven't hired anyone new into the system in five or six years. • There was severe engagement by the community leaders, but somehow, we could not follow that through with making the government-- so I think one of the major challenges that I would think is really the government not only engaged by accepting that is their work, but actually to get funded. So, government funding is limited. And government implementation or what they have agreed to do is significantly limited.

Table 2 summarizes the most consistent lessons learned/ recommendations highlighted across country programs for each of the primary themes. Select quotes from different respondents are included to support our recommendations. Quotes have been anonymized.

Country (approximate population size and total births): Liberia (population 5 million; 165,000 annual births)

Province or city where the program took place (approximate population size and total births): Greater Monrovia (population 1 million; 33,000 annual births)

Approximate planning period and duration of screening: 2 years planning beginning 2010; 21 months screening

Number of birth centers involved at any stage in the duration of the program: 1

Timing of screening: In the days following birth

Approximate numbers of babies screened: 3,986

Location of laboratory and laboratory screening method: Noguchi Memorial Institute for Medical Research, University of Ghana, Legon; initial screening method: testing by IEF

Main partners involved: Thrasher Research Fund; Boston Children's Hospital; John F. Kennedy Hospital, Monrovia

Status (2021): Screening paused due to Ebola epidemic and limited funding; planning to resume screening with support from ASH CONSA

Country (approximate population size and total births): Ghana (population 30 million; 870,000 annual births)

Province or city where the program took place (approximate population size and total births): Mainly Kumasi and surrounding districts (population 3.3 million; 96,000 annual births) and one site in Accra (population 2.5 million; 73,000 annual births)

Approximate planning period and duration of screening: 4 years planning beginning 1991; 25 years screening

Number of birth centers involved at any stage in the duration of the program: 39

Timing of screening: In the days following birth; if missed, then at the first well-baby visit (approximately 2-4 weeks of age)

Approximate numbers of babies screened: 523,159 as of June 30th 2020

Location of laboratory and laboratory screening method: Noguchi Memorial Institute for Medical Research, University of Ghana, Legon Accra; IEF for screening and HPLC for confirmatory testing (however, unaffordability of HPLC reagents led to testing by IEF only)

Main partners involved: Sickle Cell Foundation of Ghana; US National Institutes of Health; Ghana and Brazilian government; Pfizer (supporting NBS at Korle Bu Teaching Hospital, Accra, since 2017); ASH CONSA (supporting 37 Military and Greater Accra Regional Hospitals since Dec 2020)

Status (2021): Active; reduced funding has forced reduction in screening sites (to 6 in 2021)

Country (approximate population size and total births): Angola (population 32 million; 1.3 million annual births)

Province or city where the program took place (approximate population size and total births): Luanda Province (population 7 million; 287 annual births) and Cabinda Province (population 800,000; 33,000 annual births)

Approximate planning period and duration of screening: 1-2 years planning beginning 2011; 10 years screening

Number of birth centers involved at any stage in the duration of the program: Initially 2 large maternity hospitals in Luanda province with expansion to 22 health centers with maternity wards in Luanda and Cabinda province

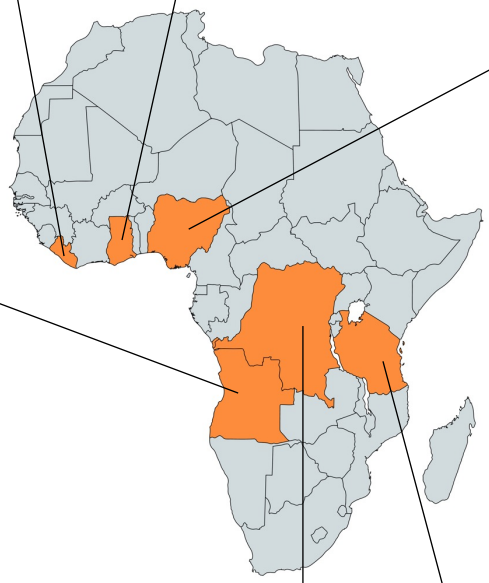
Timing of screening: In the days following birth

Approximate numbers of babies screened: 485,955

Location of laboratory and laboratory screening method: Centralized laboratory within the public pediatric hospital in Luanda utilizing IEF

Main partners involved: Texas Children's Hospital, Angola MoH, Chevron corporation

Status (2021): Paused; Chevron and Texas Children's funding/support completed in June 2020; MoH working to transition to public ownership



Country (approximate population size and total births): Nigeria (population 201 million; 7.6 million annual births)

Province or city where the program took place (approximate population size and total births): Kaduna (population 1.1. million; 42,000 annual births), Katsina (population 505,000; 19,000 annual births), and Abuja (population 1.2 million; 46,000 annual births)

Approximate planning period and duration of screening: 9 months planning beginning 2010; 18 months screening

Number of birth centers involved at any stage in the duration of the program: 4

Timing of screening: Ranged from the days following birth to 6 months of age

Approximate numbers of babies screened: 660

Location of laboratory and laboratory screening method: Abuja-Zankli Medical Centre (private hospital); HPLC (Classic model)

Main partners involved: Kafanchan and Zankli Medical Centre (Abuja), Guy's and St Thomas NHS Trust, UK; Michigan State University, US; NGO Fantsuam Foundation

Status (2021): Re-starting with EU funded project (African Research and Innovative Initiative for Sickle cell Education and ASH CONSA)

Country (approximate population size and total births): Democratic Republic of Congo (population 87 million; 3.6 million annual births)

Province or city where the program took place (approximate population size and total births): Mainly Kinshasa (population 17 million; 697,000 annual births) and also involving 3 additional provinces: Bas Congo, Kasai, Katanga (total population 14.3 million; 586,000 annual births)

Approximate planning period and duration of screening: 2 years planning beginning 2005; 14 years screening

Number of birth centers involved at any stage in the duration of the program: 262

Timing of screening: In the days following birth, in children under age 5 in tandem with an immunization program, or when newly diagnosed patients required transfusion

Approximate numbers of babies screened: Greater than 180,000 newborns and a total of more than 230.000 young children

Location of laboratory and laboratory screening method: Centre Hospitalier Monkole/Centre de Formation et d'Appui Sanitaire (CEFA) in Kinshasa and an antenna laboratory in Lubumbashi/ Katanga; IEF for screening and capillary electrophoresis for confirmatory testing

Main partners involved: Centre Hospitalier Monkole/Centre de Formation et d'Appui Sanitaire (CEFA); European Union; Agence Française de Développement (AFD), DGD Coppération Belge; Pierre Fabre Foundation; Association for Cultural, Technical, and Educational Cooperation/Belgium (ACTEC) ; Institut Européen de Coopération et de Développement/France (IECD) ; Instituto per la Cooperazione Universitaria, Italy (ICU)

Status (2021): Reduction of screening due to lack of funding

Country (approximate population size and total births): Tanzania (population 58 million; 2.1 million annual births

Province or city where the program took place (approximate population size and total births): Dar-es-Salaam (population 4.4 million; 163,000 annual births) and Mwanza (population 2.8 million; 104,000 annual births)

Approximate planning period and duration of screening: 1 year planning beginning 2015; 24 months of screening

Number of birth centers involved at any stage in the duration of the program: 3

Timing of screening: In the days following birth

Approximate numbers of babies screened: 6,000

Location of laboratory and laboratory screening method: Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania; Isoelectric focusing and HPLC

Main partners involved: Muhimbili University of Health and Allied Sciences

Status (2021): Active through research activities (Fogarty K43 Emerging Global Leader Award and the Sickle Pan-African Research Consortium) and health projects (ASH CONSA)

Supplemental Materials

I. Background questions

Questions sent by email ahead of interview and discussed at the start of each interview

a. In what city or geographic region was/is the program?

b. What is the approximate population size of the catchment area(s) covered?

c. About how long was the program planning process before screening started?

d. When did screening start?

e. Did the program end or is it ongoing?

f. If it ended, how long did it run for?

g. How babies were, or have been, screened in total?

h. How many birth centers were/are involved in the program?

II. Interview guide: Phase one

INTRODUCTION

Thank you for speaking with me today. My name is [name here]. As I mentioned in our email exchange, we are doing a study to inform success of newborn screening programs in Africa by assessing enablers and barriers to these programs by learning from the experiences of programs that had been established in the past and programs that are ongoing.

Over the next few months we aim to speak with representatives from various programs. Our plan is to distill the learnings into a format that can be used practically by various stakeholders including health workers, policy makers, NGOs, and others. We anticipate a publication, which we would invite you to review and take part in.

Note that this project received Institutional Review Board (IRB) exemption from the Boston Children's Hospital. We won't be asking for any patient information.

Today, I'd like to learn about your experience with the SCD newborn screening program in [country]. By agreeing to this interview, it is understood that you are in a position to comment on the newborn screening program that took place there and have the necessary authorization to speak on behalf of the program.

Would it be ok for me to audio-record the interview? That will help be sure we don't miss anything when we do the analyses. In the write-up, we won't attribute any specific statements to you unless we get your permission for that.

Any questions or comments?

Thank you so much again. Ok—let's get started with the interview, which will take about 45 minutes.

INTERVIEW

1. Email survey questions

If any email survey questions not answered or need clarification—ask those first. If all have been answered, then move on to next section.

2. Partners

- Who were all the partners involved in the program?
  [Govt, MOH, University, teaching hospital, NGO, professional societies, consultants, other]
  [Categorize: local partner vs international partner]

- Which partner or partners would you say had the biggest role in planning the program? Can you describe their role?

- Which partner or partners would you say had the biggest role in running the program? Can you describe their role?

- What were the main roles of the other partners?
  [Ask specifically about role of government/MOH]

- What was it like to get buy-in from the other partners? What was your approach? Could you tell me more?

3. Planning

- How did the idea for the program come about in the first place?

- What was helped the program most in the planning phase?

- What was the biggest challenge you faced in the planning phase?

- Was it envisioned at the start as a "pilot" program with a defined endpoint? Could you tell me more about that?

4. Launch

- Was there some sort of launch event when screening started?

- If so, was that important? What did the launch event consist of? Could you tell me more about that?

5. Logistics

- Who managed the day-to-day operation of the program?
  [Profile of managers (nurse, doctor, etc), team composition (how many), full-time/part-time]

- Was there a "headquarters" for the newborn screening program? If so, where was it located?

- Could you describe the birth centers where newborn screening took place?
  [Clinics, hospital, urban, rural]

- Were babies screened before leaving facility, or did they return for screening at a later date? How do you think this affected the success of the program?

- Who did most of the heelsticks? About how many participated in the program?
  [Want to learn how many nurses and/or other health workers were trained/participated in the program in the various birth centers where screening took place]

- Was there a consent process for families before obtaining heelstick? If so, could you please describe it?

- Could you briefly describe the sample collection and transport process from the point of heelstick to the screening laboratory? Were there any major problems in handling the samples?

- *How did patient information get to the screening lab? How did results get back to patients?* Did you use a specific computer program to manage information—if so, which one? Were there any major problems in collecting or managing data/information?

- What in your opinion were the most important factors that led to success in day-to-day operation of the program?

- What were the biggest challenges in day-to-day operation of the program?

- Were modifications to the way the program ran made over time?

6. Laboratory

- Was a SCD screening lab newly set up in conjunction with the screening program, or was an already established SCD screening lab used? Was the lab located in the same facility where screening occurred? How did that affect success?

- Who worked in the laboratory to analyze the samples?
[Profile of staff (techs, etc), team composition (how many), full-time/part-time]

- Did the lab have equipment problems? Staffing problems? Could you tell me more? [*How did this affect how the lab ran?]*

- What method was used to conduct the screening test?
[For example, isoelectric focusing]

- Do you happen to know what specific equipment was used in the lab?
[E.g., brand name of isoelectric focusing machine]

- What was the most important factor in the successful running of the lab?

- What was the biggest barrier to running the lab?

7. Notification and follow-up

- If a baby screened positive, how were the parents notified? Who did that communication? What messages were delivered?

- What was the process for babies that screened positive—for example, did they get enrolled in a clinical management program? Could you tell me more about that? *[Seeking details of the sickle cell management program, if there was one]*

8. Funding

- How was the program funded? Were the costs shared by different parties

- What were/are the parts of the program that are most expensive?

- Would you be comfortable sharing the approximate cost of the program?
[Start-up costs, annual running costs]

- How did costs affect the program? *[were activities, services, scale, sustainability etc. affected for financial reasons?]*

9. Program disposition

- **If the program has ended**—did it end when planned, go for longer than planned, or end prematurely? What do you think were the main reasons for this?

- **If the program is ongoing**—has it remained stable size, grown, or diminished in size? What do you think have been the main reasons for this?

10, Perceptions

- How did you and the other leaders of this program define [and measure] success?

- Could you comment on how families viewed the program? Could you tell me more about that? [*if viewed negatively, how did the program deal with that?]*

- What was your own biggest learning in doing this program?

11. Closing

- Are there any reports or publications about the program that could be shared with me?

- Is there anything else that you think I should know that we didn't talk about?

- Based on the interviews, we'll be writing a report summarizing the findings and we would like to acknowledge your contribution. Is that ok? We will share the report with you when it's ready and it would be great to get your feedback.

- In addition to you, we have also spoken with Dr. [name] from [country, Dr [name] from [country], etc. Are you aware of other newborn screening programs in Africa and contacts that we haven't yet connected with?

Thank you very much for speaking with me.

Bye!

III. Main topic categories for phase two interviews

For each, discussing how it impacted success, challenges, enablers, and other lessons learned.

- Cultural issues (among providers and community)
- Sustainability
- Balance of involvement between external and local partners
- Notification and follow up

IV. Interview guide: Phase two

INTRODUCTION

Thank you for speaking with me today. My name is Natalie. As I mentioned in our email exchange, we are doing a study to inform success of NBS programs in Africa by assessing enablers and barriers to these programs by learning from the experiences of programs that had been established in the past and programs that are ongoing.

Over the next few months we aim to speak with representatives from various programs. Our plan is to distill the learnings into a format that can be used practically by various stakeholders including health workers, policy makers, NGOs, and others. We anticipate a publication, which we would invite you to review.

Note that this project received Institutional Review Board (IRB) exemption from the Boston Children's Hospital. We won't be asking for any patient information.

Today, I'd like to learn about your experience with the SCD newborn screening program in [country]. By agreeing to this interview, it is understood that you are in a position to comment on the NBS program that took place there and have the necessary authorisation to speak on behalf of the program.

Would it be ok for me to audio-record the interview? That will help be sure we don't miss anything when we do the analyses. In the write-up, we won't attribute any specific statements to you unless we get your permission for that.

Any questions or comments?

Thank you so much again. Ok—let's get started with the interview, which will take about 45 minutes.

INTERVIEW

1. Email survey questions

If any email survey questions not answered or need clarification—ask those first. If all have been answered, then move on to next section.

2. Partners

Who were the partners involved in the program?

- What was the role of local leaders and champions in the program?
- What was the role of external partners?
- What was the role of the government?

- How did they affect the success of the program?
- What lessons learned or recommendations do you have about working with partners?

3. Logistics

- Can you please walk me through the entire screening process for one baby starting with how the baby is identified through how the parents are notified?
    - Probes: data management systems, equipment and supplies needed, getting results back to patients

- What in your opinion were the most important factors that led to success in day-to-day operation of the program?

- What were the biggest challenges in day-to-day operation of the program?

- What lessons learned or recommendations do you have about running the day to day operations of the program?

- Probe: challenges and facilitators for running the lab, recommendations

4. Program disposition

- **If the program has ended**—did it end when planned, go for longer than planned, or end prematurely? What do you think were the main reasons for this?
    - What would be needed in order to have a sustainable program?

- **If the program is ongoing**—has it remained stable size, grown, or diminished in size? What do you think have been the main reasons for this?

- Who pays for it?

- What recommendations do you have for other programs in the planning and implementation phase that can set them up to be sustainable?

5. Perceptions

- Could you comment on how families and the community viewed the program? Could you tell me more about that? [*if viewed negatively, how did the program deal with that?]*
    - *Probes: stigma, need for education*

- How did this impact the success of the program?

- What was your own biggest learning from the program?

6. Closing

- Are there any reports or publications about the program that could be shared with me?

- Is there anything else that you think I should know that we didn't talk about?

- Based on the interviews, we'll be writing a report summarizing the findings and we would like to acknowledge your contribution. Is that ok? We will share the report with you when it's ready and it would be great to get your feedback.

Thank you very much for speaking with me.

Bye!

SRQR for Archer et al., *Enablers and barriers to newborn screening for sickle cell disease in Africa: results from a qualitative study involving programs in six countries*

Standards for Reporting Qualitative Research (SRQR)*

Title and abstract		**Page/line no(s).#**
	Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	p.1 lines 3-4
	Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	p. 2
Introduction		
	Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	p. 4 lines 3-43
	Purpose or research question - Purpose of the study and specific objectives or questions	p. 4 lines 48-51 p. 5 lines 7-10
Methods		
	Qualitative approach and research paradigm - Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale**	p. 5 lines 7-10
	Researcher characteristics and reflexivity - Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability	p. 6, lines 9-15
	Context - Setting/site and salient contextual factors; rationale**	p. 6, line 8
	Sampling strategy - How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale**	p. 5 lines 16-27, 32-25
	Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	p. 6 lines 27-29
	Data collection methods - Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale**	p. 5, lines 16-25 p. 6, lines 6-9
	Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	p. 5, lines 44-51 p. 6, lines 1-3
	Units of study - Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	p. 6, lines 34-38 Figure 1

	Data processing - Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/de-identification of excerpts	p. 6, lines 8-16
	Data analysis - Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale**	p. 6, lines 17-24
	Techniques to enhance trustworthiness - Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale**	p. 5, Lines 35-39
Results/findings		
	Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	p. 6-9 Table 1. Summary of main results Table 2. Major lessons learned
	Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	Table 2. Participant quotes
Discussion		
	Integration with prior work, implications, transferability, and contribution(s) to the field - Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	p. 9-10
	Limitations - Trustworthiness and limitations of findings	p.10, lines 17-26
Other		
	Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	p. 10, lines 46-51 p. 11, lines 1-2
	Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	p. 11, lines 12-14

*Reference: O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. *Academic Medicine*, Vol. 89, No. 9 / Sept 2014. DOI: 10.1097/ACM.0000000000000388. Accessible at: http://www.equator-network.org/reporting-guidelines/srqr/.

**The authors of the above reference created the SRQR by searching the literature to identify guidelines, reporting standards, and critical appraisal criteria for qualitative research; reviewing the reference lists of retrieved sources; and contacting experts to gain feedback. The SRQR aims to improve the transparency of all aspects of qualitative research by providing clear standards for reporting qualitative research.

***The rationale should briefly discuss the justification for choosing that theory, approach, method, or technique rather than other options available, the assumptions and limitations implicit in those choices, and how those choices influence study conclusions and transferability. As appropriate, the rationale for several items might be discussed together.

#Please note that we understand the line numbers may be slightly adjusted based on formatting on the paper (i.e., Word version to PDF).